

REMARKS

Claims 25-28 are pending in this application. Claims 1-24 have been cancelled as being drawn to the non-elected invention. Claims 25-28 are rejected. Claim 1 is objected to. The Examiner appears to have intended the objection to apply to claim 25, and Applicants have assumed so herein. Applicants cancel claim 27 herein without prejudice or disclaimer. Applicants amend claims 25, 26, and 28 herein. Support for amended claims 25, 26, and 28 can be found at pages page 6, lines 22-28 and page 12 of the specification. Thus, no new matter is added.

In view of the following amendment and response, Applicants believe the claims presented herein are allowable. Reconsideration is respectfully requested.

SEQUENCE COMPLIANCE

The Examiner alleges that the application fails to provide sequence numbers for short amino acid sequences disclosed on page 13 and 15 of the specification. Applicants have herein amended the specification to include sequence identifiers for the amino acid sequences having at least four amino acids as required by 37 CFR 1.821(a)(1). These amino acid sequences that contain four or more amino acids are disclosed on pages 13 and 15 of the specification. In addition, Applicant submits herein a corresponding sequence listing. Both a paper and electronic copy of the sequence listing is also sent to Mailstop: Sequence on a computer readable diskette.

CLAIM OBJECTIONS

Claim 1 is objected to for containing the term "sn-2." Applicants respectfully submit that it appears as though the Examiner intended to refer to claim 25 and addresses that objection based on that assumption. Applicants respectfully submit that the term "sn-2 ester" is presented on page 1, line 13 of the application as well throughout the application. In addition, this term is well understood in the art. For instance, the term is used in

Steinbrecher, *et al.* (*Journal of Lipid Research*, Vol. 30(3): 305-315 (1989))(hereinafter referred to as "Steinbrecher, et al.") or Stremler, *et al.* (*Journal of Biological Chemistry*, Vol. 264(10): 5331-5334 (1989))(hereinafter referred to as "Stremler et al."), which are two references cited by the Examiner in the Office Action. Thus, Applicants have not amended the term in claim 25 but respectfully submit that the claim is in condition for allowance.

REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 25 and 26-27 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner alleges that the phrase "an active enzyme" is not clear. The Examiner alleges that the specification does not provide a specific definition for the phrase.

Applicants traverse this rejection. Applicants respectfully submit that both the specification and scientific literature are replete with definitions of enzyme activity. For instance, the specification describes enzyme activity as relating to the activity of purified enzyme on page 9, lines 8-14 of the specification. Applicants also provide methods for measuring enzyme activity in the examples on pages 10 and 16 of the specification. In addition, Applicants respectfully submit that both Steinbrecher, *et al.* and Stremler, *et al.*, which are cited by the Examiner in the Office Action, present active assays that are known in the art and can be applied to PAF acetylhydrolase activity. See page 307 of Stremler, *et al.* and page 5332 of Steinbrecher, *et al.*

Furthermore, Applicants respectfully submit that when determining whether a claim satisfies the requirements of 35 U.S.C. 112, second paragraph, one must determine "whether those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.* 1 U.S.P.Q.2d. 1081, 1088 (Fed. Cir. 1986) See also *North Am. Vaccine, Inc. v. American Cyanamide Co.* 28

U.S.P.Q.2d. 1333, 1339 (Fed. Cir. 1993). A definition of an active enzyme is well understood in the art and disclosed for a plethora of enzymes in the literature, including assays for PAF acetylhydrolase activity by Stremler, *et al.* and Steinbrecher, *et al.* Therefore, Applicants have not amended the term in claims 25 and 26. Claim 27 is canceled herein, thus rendering rejection of this claim moot.

The Examiner also alleges that claims 25 and 26-27 are indefinite for reciting the phrase "enzyme lipoprotein associated" The Examiner suggests deletion of the term, "enzyme." Applicants have deleted the term "enzyme" in claims 25 and 26. Claim 27 is canceled herein, thus rendering rejection of this claim moot.

Claim 26 stands rejected under 35 U.S.C. §112, second paragraph. The Examiner alleges that the term "feature" is not clear, and indicates that the term "sequence" may be intended. Applicants have amended claim 26 herein to replace the word "feature" with the word "sequence." Furthermore, the Examiner suggests that the group of SEQ ID NOs should be "inclusive." Applicants have amended the group to recite "SEQ ID NO:1, 2, and 4." Applicants have removed SEQ ID NOs: 10 and 11 from claim 26.

Claims 27 also stands rejected under 35 U.S.C. §112, second paragraph. Claim 27 is canceled herein, thus rendering rejection of this claim moot.

Claim 28 stands rejected under 35 U.S.C. §112, second paragraph. In particular, the Examiner alleges that the phrase "nucleic acids 929 to 1018 of SEQ ID NO:9" is unclear. The Examiner alleges that Applicants appear to mean "nucleotides 929 to 1018 of SEQ ID NO:9." Applicants have amended the term "nucleic acids" to "nucleotides" herein.

Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, Applicants have overcome the Examiner's rejection under 35 U.S.C. §112, second paragraph, and the rejection should be withdrawn.

REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 25-28 are rejected under 35 U.S.C. §112, first paragraph. The Examiner alleges that "the specification, while being enabling for a lipoprotein associated phospholipase A2 (LPA-PLA2) having a molecular weight of from about 45-50 kDa and comprising amino acid sequence encoded by SEQ ID NO:9, does not reasonably provide enablement for any or all such LPA-PLA2 from any or all sources including polypeptides comprising fragments, variant, mutants and recombinants." The Examiner also alleges that claims 25-28 "are so broad as to encompass any LPA-PLA2 from any or all sources and enzyme comprising fragments."

Applicants have herein amended claim 25 to include the phrase "naturally occurring human" in describing "lipoprotein associated phospholipase A2." Applicants respectfully submit that the phrase "naturally occurring human" is well understood in the art. However, Applicants have also provided within the specification methods for isolating the encoding nucleic acids of the invention through a human genomic library. See page 6, lines 22-28 of the specification. Furthermore, Example 4 provides a method for purifying "native" LPA-PLA2 from human plasma. See page 12 of the specification. The skilled artisan would understand the connection between "native" and "naturally occurring" human LPA-PLA2.

As Applicants have limited the scope of claims 25 and 28 to include only "naturally occurring human" forms of LPA-PLA2, Applicants respectfully submit that these claims do not cover the various constructs and mutants that form the grounds of the Examiner's rejection. Applicants respectfully submit that they provide sufficient guidance to enable one skilled in the art to make and use the claimed invention as claims 25 and 28 are now directed to LPA-PLA2 in naturally occurring human forms.

Applicants respectfully submit that as claim 26 depends from claim 25 it contains all of the limitations of claim 25 and is now in condition for allowance based on the

amendments made to claim 25. Furthermore, claim 27 is canceled herein, thus rendering rejection of this claim moot.

Claims 25 also stands rejected under 35 U.S.C. §112, first paragraph, for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed had possession of the claimed invention. In particular, the Examiner alleges that claim 25 is directed to LPA-PLA2 polypeptides from "all sources."

Applicants respectfully submit that claim 25 has been amended to recite "naturally occurring human lipoprotein associated phospholipase A2." As discussed above, the specification provides support for this amendment. Applicants submit that claim 25 no longer encompasses LPA-PLA2 from all sources and includes only naturally occurring forms and mutations from human. In addition, both claims 25 and 28 recite a level of purity for LPA-PLA2 and an additional chemical or physical characteristic describing LPA-PLA2. For instance, claim 25 describes the enzyme activity of LPA-PLA2, and claim 28 describes the nucleic acid sequence encoding LPA-PLA2.

Claims 25-28 stand rejected under 35 U.S.C. §112, first paragraph. In particular, the Examiner alleges that these claims are "directed to a genus of polypeptides having acetylhydrolase activity and comprising amino acids of SEQ ID NO:1, 2 , 4, 10 or amino acids encoded by fragments of SEQ ID NO:9 such as nucleotides 929-1018." The Examiner alleges that specification does not contain any disclosure of "the structure of all polypeptides included in the claimed genera."

Applicants respectfully submit that "a patent need not teach and preferably omits, what is well known in the art." *Lindemann Maschinenfabrik v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1563 (Fed Cir. 1984). Applicants traverse this rejection as the Examiner appears to require that Applicants disclose within the specification every possible

amino acid or nucleic acid sequence that could contain the sequences recited in claims 26 and 28 and still demonstrate all other limitations recited within claims 25 and 26 or 28.

Such a requirement is analogous to requiring that a claim, directed to an isolated polynucleotide within an expression vector, recite all possible expression vectors that could comprise the isolated sequence. Applicants respectfully submit that they are not required to disclose or provide an example of all possible members of a genus in order to claim the genus as long as they have reasonably conveyed to the skilled artisan how to make or use the invention.

The claims recite a genus wherein each member of the genus possesses physical and chemical characteristics shared by other members, *viz.* a specific sequence, purity level and enzymatic activity. These claims, read in light of the specification, would teach the skilled artisan how to make and use the species of the genus.

Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, Applicants have overcome the Examiner's rejection under 35 U.S.C. §112, first paragraph, and the rejection should be withdrawn.

REJECTIONS UNDER 35 U.S.C. §102(b)

Claims 25-28 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Steinbrecher, *et al.* (*Journal of Lipid Research*, Vol. 30(3): 305-315 (1989))(hereinafter referred to as "Steinbrecher") or Stremler, *et al.* (*Journal of Biological Chemistry*, Vol. 264(10): 5331-5334 (1989))(hereinafter referred to as "Stremler").

Inherent anticipation arises when "the prior art *necessarily* functions in accordance with, or includes, the claimed limitations," *Atlas Powder Co v. IRECO Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999). Emphasis added. Applicants respectfully traverse these rejections.

As the Examiner concedes, neither of the cited references disclose any amino acid or nucleotide sequences. The Examiner alleges that "based on the activity and the source of

the enzyme" in each reference "the amino acids are inherent characteristics and therefore the enzymes in the reference and the instant enzyme claimed are one and the same."

Applicants respectfully submit that enzymes with similar activities and derived from the same source can have varied amino acid sequences. For instance, Campbell, *et al.* (WO 02/36817, SmithKline Beecham PLC) describe polymorphisms or naturally occurring variations in DNA sequences within an organism which may or may not manifest in an observed phenotype. Specifically, Campbell, *et al.*, describe polymorphisms that naturally occur within LPA-PLA2 at position 379. Furthermore, Campbell, *et al.* also cite Cousens, *et al.* (WO 95/09921, ICOS Corporation) which discloses another known polymorphism of LPA-PLA2 at position 279.

Because polymorphisms are known to occur naturally in Lp-PLA2 from human, Applicants respectfully submit that it is not reasonable to assume that the sequences of polypeptides disclosed in Steinbrecher, *et al.* or Stremler, *et al.* would be identical to each other or to the sequences claimed in the instant application. Therefore, these two references cannot inherently anticipate the claims of the present case as they do not necessarily include the claim limitations.

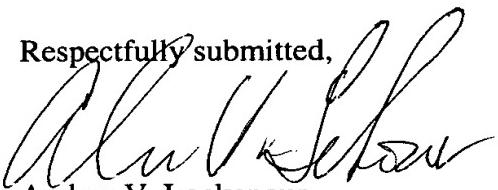
Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, Applicants have overcome the Examiner's rejection under 35 U.S.C. §102(b), and the rejection should be withdrawn.

DOUBLE PATENTING REJECTION

Claims 25-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No 5,981,252. Applicants submit a Terminal Disclaimer filed with this response.

Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited.

If it would expedite the prosecution of this application, the Examiner is invited to confer with Applicants' undersigned attorney.

Respectfully submitted,

Andrea V. Lockenour
Attorney for Applicants
Registration No. 51,962

GlaxoSmithKline
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939
Phone (610) 270-7568
Facsimile (610) 270-5090
N:\AVL\patapps\P306934C4X1\X1C1 ROA1.doc